EXAMINER SEARCH NOTES

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     (FILE 'HOME' ENTERED AT 17:09:02 ON 03 JUL 2005)

     FILE 'REGISTRY' ENTERED AT 17:10:15 ON 03 JUL 2005
L1           143 TETRAHYDROCANNABINOL
L2           128 S L1/CNS
L3             0 S /DELTA. 8-TETRAHYDROCANNABINOL/CNS
L4            41 S Δ8-TETRAHYDROCANNABINOL/CNS
L5            24 S CANNABINOL/CNS
L6            42 S CANNABIDIOL
L7            17 S CANNABIDIOL/CNS

     FILE 'REGISTRY' ENTERED AT 17:15:46 ON 03 JUL 2005
                SET TERMSET E#
                DEL SEL Y
                SEL L7 15 RN
L8              1 S E1/RN
                SET TERMSET LOGIN

     FILE 'AGRICOLA' ENTERED AT 17:15:50 ON 03 JUL 2005
L9             23 S L8

     FILE 'REGISTRY' ENTERED AT 17:16:04 ON 03 JUL 2005

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS, CANCERLIT' ENTERED AT 17:18:04 ON
     03 JUL 2005
L10        155028 S BRAIN TUMOR OR BRAIN CANCER OR BRAIN NEOPLASM
L11          3450 S CANNABIDIOL
L12             0 S L10 (10A) L11
L13             3 S L10 AND L11
L14          1105 S Δ8-TETRAHYDROCANNABINOL
L15             1 S L10 AND L14
L16          3450 S CANNABIDIOL
L17             3 S L10 AND L16

     FILE 'USPATFULL' ENTERED AT 17:24:24 ON 03 JUL 2005
L18          7125 S L10
L19           108 S L11
L20             1 S L18 AND L19
L21            24 S L14
L22             1 S L10 AND L21
L23             1 S L18 AND L21
L24           108 S L16
L25             1 S L18 AND L24

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L30 ANSWER 13 OF 15 CANCERLIT on STN DUPLICATE 8
AN 2000165227 CANCERLIT
DN 20165227 PubMed ID: 10700234
TI Anti-tumoral action of **cannabinoids**: involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation.
CM Comment in: Nat Med. 2000 Mar;6(3):255-6
AU Galve-Roperh I; Sanchez C; Cortes M L; del Pulgar T G; Izquierdo M; Guzman M
CS Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, 28040-Madrid, Spain.
SO NATURE MEDICINE, (2000 Mar) 6 (3) 313-9.
Journal code: 9502015. ISSN: 1078-8956.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2000165227
EM 200003
ED Entered STN: 20000413
Last Updated on STN: 20000413
AB Delta9-Tetrahydrocannabinol, the main active component of marijuana, induces apoptosis of transformed neural cells in culture. Here, we show that intratumoral administration of Delta9-tetrahydrocannabinol and the synthetic cannabinoid agonist WIN-55,212-2 induced a considerable regression of malignant gliomas in Wistar rats and in mice deficient in recombination activating gene 2. Cannabinoid treatment did not produce any substantial neurotoxic effect in the conditions used. Experiments with two subclones of C6 glioma cells in culture showed that **cannabinoids** signal apoptosis by a pathway involving cannabinoid receptors, sustained ceramide accumulation and Raf1/extracellular signal-regulated kinase activation. These results may provide the basis for a new therapeutic approach for the treatment of malignant gliomas.

L30 ANSWER 14 OF 15 CANCERLIT on STN DUPLICATE 9
AN 2000200551 CANCERLIT
DN 20200551 PubMed ID: 10734181
TI Synthesis and characterization of a fluorescent substrate for the N-arachidonoylethanolamine (anandamide) transmembrane carrier.
AU Muthian S; Nithipatikom K; Campbell W B; Hillard C J
CS Department of Pharmacology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA.
NC DA09155 (NIDA)
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2000 Apr) 293 (1) 289-95.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2000200551
EM 200004
ED Entered STN: 20000515
Last Updated on STN: 20000515
AB N-Arachidonoylethanolamine (AEA) is a proposed endogenous ligand of the central cannabinoid receptor (CB1). Previous studies indicate that AEA is translocated across membranes via a process that has the characteristics of carrier-mediated facilitated diffusion. To date, studies of this mechanism have relied on [(3)H]AEA as a substrate for the carrier. We have synthesized an analog of AEA, SKM 4-45-1, that is nonfluorescent in the extracellular environment. When SKM 4-45-1 is exposed to intracellular esterases, it is de-esterified and becomes fluorescent. We have carried out studies to demonstrate that SKM 4-45-1 accumulation in cells occurs via the AEA carrier. SKM 4-45-1 is accumulated by both cerebellar granule cells and C6 glioma cells. Uptake of SKM 4-45-1 into C6 glioma is inhibited by AEA (IC(50)=53.8 +/- 1.8 microM), arachidonoyl-3-aminopyridine amide (IC(50)=10.1 +/- 1.4 microM), and arachidonoyl-4-hydroxyanilineamide (IC(50)=6.1 +/- 1.3 microM), all of which also inhibit

[(3)H]AEA accumulation. Conversely, [(3)H]AEA accumulation by cerebellar granule cells is inhibited by SKM 4-45-1 with an IC(50) of 7.8 +/- 1. 3 microM. SKM 4-45-1 is neither a substrate nor inhibitor of fatty acid amide hydrolase, an enzyme that catabolizes AEA. SKM 4-45-1 does not bind the CB1 cannabinoid receptor at concentrations <10 microM. In summary, the cellular accumulation of SKM 4-45-1 occurs via the same pathway as AEA uptake and provides an alternative substrate for the study of this important cellular process.

L30 ANSWER 15 OF 15 CANCERLIT on STN DUPLICATE 10
AN 1999042008 CANCERLIT
DN 99042008 PubMed ID: 9822713
TI Anandamide hydrolysis by human cells in culture and brain.
AU Maccarrone M; van der Stelt M; Rossi A; Veldink G A; Vliegenthart J F; Agro A F
CS Department of Experimental Medicine and Biochemical Sciences, University of Rome Tor Vergata, Via di Tor Vergata 135, I-00133 Rome, Italy.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Nov 27) 273 (48) 32332-9. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1999042008
EM 199812
ED Entered STN: 19990127
Last Updated on STN: 19990127
AB Anandamide (arachidonylethanolamide; AnNH) has important neuromodulatory and immunomodulatory activities. This lipid is rapidly taken up and hydrolyzed to arachidonate and ethanolamine in many organisms. As yet, AnNH inactivation has not been studied in humans. Here, a human brain fatty-acid amide hydrolase (FAAH) has been characterized as a single protein of 67 kDa with a pI of 7.6, showing apparent Km and Vmax values for AnNH of 2.0 +/- 0.2 microM and 800 +/- 75 pmol.min-1.mg of protein-1, respectively. The optimum pH and temperature for AnNH hydrolysis were 9.0 and 37 degreesC, respectively, and the activation energy of the reaction was 43.5 +/- 4.5 kJ.mol-1. Hydro(pero)xides derived from AnNH or its linoleoyl analogues by lipoxygenase action were competitive inhibitors of human brain FAAH, with apparent Ki values in the low micromolar range. One of these compounds, linoleoylethanolamide is the first natural inhibitor (Ki = 9.0 +/- 0.9 microM) of FAAH as yet discovered. An FAAH activity sharing several biochemical properties with the human brain enzyme was demonstrated in human neuroblastoma CHP100 and lymphoma U937 cells. Both cell lines have a high affinity transporter for AnNH, which had apparent Km and Vmax values for AnNH of 0.20 +/- 0.02 microM and 30 +/- 3 pmol.min-1.mg of protein-1 (CHP100 cells) and 0.13 +/- 0.01 microM and 140 +/- 15 pmol.min-1.mg of protein-1 (U937 cells), respectively. The AnNH carrier of both cell lines was activated up to 170% of the control by nitric oxide.

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